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COLACE AND OTHER WETTING AGENTS FOR CONSTIPATION

When excessive absorption of water from the stool in functional constipation produces a hard fecal mass, a laxative agent which softens the stool without irritating the intestinal tract is often helpful. Mineral oil is such an agent, and it has been widely and safely used for many years.

Five years ago, the first of a number of papers appeared reporting the successful use of "surface-acting" or "wetting" agents for functional constipation (J. L. Wilson and D. C. Dickinson, JAMA, 158:261, 1955). The first drug of this type to be marketed for the treatment of constipation was dioctyl sodium sulfosuccinate (Colace - Mead Johnson; and many other brands). Another wetting agent, oxyethylene oxypropylene polymer (Polykol - Upjohn; Magnocyl - Elder) is now being offered for the same purpose. Both drugs are claimed to be non-absorbable, non-toxic, and pharmacologically inert. Their action is attributed solely to their surface-acting property; by lowering surface tension, it is claimed, they permit the intestinal fluids to penetrate the fecal mass more readily, and thus to produce soft, easily passed stools.

CLINICAL STUDIES - The early enthusiastic reports on these agents still await confirmation by controlled studies; one controlled study (J. Rendle-Short, Lancet, 2:1189, 1956) found dioctyl sodium sulfosuccinate ineffective against both fecal impaction and as a routine aperient. The significance of the study is difficult to assess, however, since the number of subjects with fecal impaction was admittedly very small, and since the wetting agents are not claimed to be effective where constipation is due to inadequate bowel motility. Nevertheless, even for the prevention of fecal impaction, Medical Letter consultants consider the wetting agents to be less reliable than mineral oil. The two chief disadvantages of mineral oil - rectal leakage and interference with absorption of food and fat-soluble vitamins - can be minimized by adjustment of dosage and by having the patient take it on an empty stomach just before retiring.

In some children with tendency to fecal impaction, it is possible that oral wetting agents combined with enemas may be useful, but there is no reason to believe that they are more effective than various inexpensive laxatives. Ordinary constipation in infants and children requires psychological guidance and reassurance of the parents rather than drug treatment of the child. As for adults, mineral oil, cascara, senna, and other well-tried drugs are still effective and

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safe when dosage is adjusted to individual requirements. The wetting agents are also offered in many combination formulae containing well-tried laxative-cathartic agents such as 1, 8-dihydroxyanthraquinone, ox-bile extracts, senna, cascara and bulk-producers; their usefulness in these combinations has not been established.

The Medical Letter consultants who assisted in the preparation of this report showed a marked lack of enthusiasm for the use of wetting agents as laxatives. Mineral oil was generally considered preferable. Several called attention to the excessive use of laxatives of all kinds. Regular, daily bowel movements are not, of course, essential to good health, and reliance on laxatives to insure daily movements is much more likely to cause chronic constipation than to cure it. Long-term control of functional constipation is best achieved by appropriate diet (depending on the type of constipation) and education of the patient to disabuse him of the belief that missing a bowel movement for a day or two is harmful to health.

REAPPRAISAL OF THREE ORAL NITROFURANS

FURADANTIN - Three antibacterial agents in the group of nitrofurans, all manufactured by Eaton, have been reviewed by The Medical Letter. One of these, nitrofurantoin USP (Furadantin) (The Medical Letter, 1:37, 1959) was found to be a useful oral agent for the treatment of acute and chronic urinary-tract infections, "because of its bacteriostatic and bactericidal effectiveness against a very wide range of both gram-negative and gram-positive organisms, its relative freedom from toxicity when used orally, and the fact that its use does not encourage the growth of resistant strains."

The drug is primarily a urinary antiseptic, suppressing surface but not deep tissue infections. Further experience does not alter the Medical Letter view that Furadantin has special clinical usefulness for urinary-tract infections, particularly those in which the sulfa drugs and antibiotics cannot be used effectively or safely.

FUROXONE FOR SALMONELLA AND SHIGELLA INFECTIONS - At the time of the initial review, The Medical Letter (1:38, May 29, 1959) found too little evidence to permit acceptance of the claim that furazolidone (Furoxone) was highly effective against Salmonella and Shigella infections. Although evidence based on adequately controlled studies is still very limited, the usefulness of this drug is now better established.

In one study, S. S. Schneierson and M. Bryer (J. Mt. Sinai Hosp., 26:525, 1959) administered Furoxone to 13 patients infected with Salmonella organisms. All isolated strains of Salmonella showed in vitro sensitivity to Furoxone. A satisfactory clinical response was obtained in nine patients. An equivocal response was obtained in one case of acute typhoid fever; repeated treatment failed to eradicate the organism in two chronic carriers. Because clinical and bacteriologic results from the use of chloramphenicol and tetracyclines in Salmonella infections have often been disappointing (N. K. Ordway, Bull. W.H.O., 23:73,

1960) and because of their side effects, Furoxone may be a useful alternative to these antibiotics. They are generally ineffective in chronic carriers; whether Furoxone will be more effective is not yet known.

As for Shigella infections, in one recent study M. E. Musgrave and H. C. Arm (Antib. Med. & Clin. Therapy, 7:17, 1960) treated 37 cases of acute shigellosis with Furoxone, and achieved clinical and bacteriologic cure in all patients with a dosage of 100 mg. four times a day for seven days; in the succeeding week, the stool cultures of all but two patients remained free of Shigella. All isolated strains showed in vitro sensitivity to Furoxone. In this study, as in the Schneierson-Bryer study, no toxic or side effects were seen.

Shigella infections are quite uncommon in countries with good sanitation, and most Shigella infections are self-limited. Furthermore, rapid elimination of Shigella organisms from the intestinal tract with antibacterial agents is unlikely to alter greatly the patient's clinical illness (N. K. Ordway, see above). Nevertheless, when drug treatment of a severe Shigella infection is indicated, Furoxone appears to be a valuable agent, especially against strains resistant to sulfadiazine, tetracycline, or chloramphenicol.

ALTAFUR - This drug is claimed by the manufacturer to be "effective against the majority of common pathogenic bacteria, including the antibiotic-resistant staphylococci." The Medical Letter (1:75, Oct. 2, 1959) expressed the view that furaltadone (Altafur) had not yet been given sufficient clinical trial to warrant its general use. More recent evidence does not change that judgment.

The manufacturer's reports showing that all or practically all strains of Staphylococcus aureus are sensitive to Altafur in vitro are based on minimum inhibiting concentrations of 2.9 to 8.6 mcg. per cc., with a median of 5.8 mcg. per cc. In view of the company's figures for attainable blood levels - 1.6 to 3 mcg. per cc. - there must be some doubt about the efficacy of the compound in severe systemic infections caused by staphylococcus.

Furthermore, the manufacturer's comparisons of the in vitro sensitivities of staphylococci to Altafur and to other antibacterial agents are open to question, since sensitivity testing disks containing 50 mcg. of Altafur per disk - a level far beyond those obtainable in the body - were used. In the opinion of Medical Letter consultants, Altafur is being more widely used than is warranted by available clinical data. Such wide use appears to be due, at least in part, to a lack of awareness of the high content of the drug in the testing disks, and to the common practice of accepting the size of inhibition zones as a measure of clinical efficacy.

Side effects from Altafur include gastrointestinal irritation and skin eruptions. Blood dyscrasias in three patients have been reported and several instances of diplopia due to lateral rectus palsy (improved after discontinuance of therapy) have occurred. The manufacturer has warned that alcoholic beverages taken during or within seven days after Altafur therapy can cause such side effects as precordial pain, dyspnea and urticaria. More clinical trials on carefully defined and controlled series of cases are necessary for adequate judgment of the therapeutic effectiveness and safety of Altafur.

PREVENTION OF DIAPER RASH

Diaper rash is caused by many factors, chiefly maceration of the skin by urine and feces. Sweat retention, which may also be a factor, is promoted by hot weather, tropical room temperatures and the use of impervious rubber or plastic panties. The rash is aggravated by rough diaper cloth, by marked alkalinity of the urine caused by ammonia-producing bacteria, and by soap and detergent left in the diaper. Various preparations are offered for the prevention of diaper rash.

BREMIL - Bremil (Borden), a liquid and powdered milk formula, is promoted as a milk substitute or supplement. The manufacturer also claims that the added amino acid, methionine, in Bremil "helps avoid diaper rash metabolically," but proof of the claim is lacking. About 85 per cent of the protein in cow's milk is casein, and about 3 per cent of casein is methionine - more than enough to supply the baby's needs.

HEXACHLOROPHENE AND DESITIN - Desitin Baby Lotion (Desitin Chem. Co.) contains hexachlorophene, and the manufacturer claims that this antiseptic can "protect against ammonia-producing and other common skin bacteria." Hexachlorophene is often a useful antibacterial agent in soaps and other dermatologic preparations. Its usefulness in Desitin is questionable, since it is relatively ineffective against the gram-negative ammonia-producing organisms. Moreover, it is so sparingly soluble in water that very little could be transferred from the medication on the skin to the urine in the diaper where the production of ammonia takes place. It has not been established that topical application of vitamins A and E, as contained in Desitin Baby Lotion, will "guard skin integrity."

To help prevent diaper rash, rubber panties and excessive clothing and blankets should be avoided and the effort should be made to keep the baby's room cool. Mothers should be instructed to cleanse the diaper area with tepid water, dry the skin thoroughly, and dust it with cornstarch or plain talc. Diapers smelling of ammonia may be sterilized by boiling; or instead of boiling, the diapers may be given a final rinse with a 1 per cent acetic acid solution (a 1:4 dilution of white vinegar), which will neutralize residual alkalis.

DIAPARENE - As an alternative to boiling or an acetic acid rinse, it may be worthwhile to try the widely used quaternary ammonium analogue, methylbenzethonium chloride (Diaparene - Breon; Ammorid - Kinney) as a diaper disinfectant. This agent is especially useful because of its residual antibacterial effect. Methylbenzethonium chloride should be used only after the diaper has been washed and thoroughly rinsed.

CALGON - In localities where the water is hard, laundry soaps cause the deposition of insoluble calcium and magnesium compounds in the diaper fabric, making it harsh and irritating. Water softeners such as Calgon (sodium hexametaphosphate) help protect against this difficulty. When diapers are washed with ordinary synthetic laundry detergents, however, no calcium or magnesium compounds are deposited, and no water softener is needed. Mechanical tumble-drying is one of the best ways of keeping diapers soft.

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